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Ambient Water Quality Criteria Document Addendum for Chlorinated Phenols

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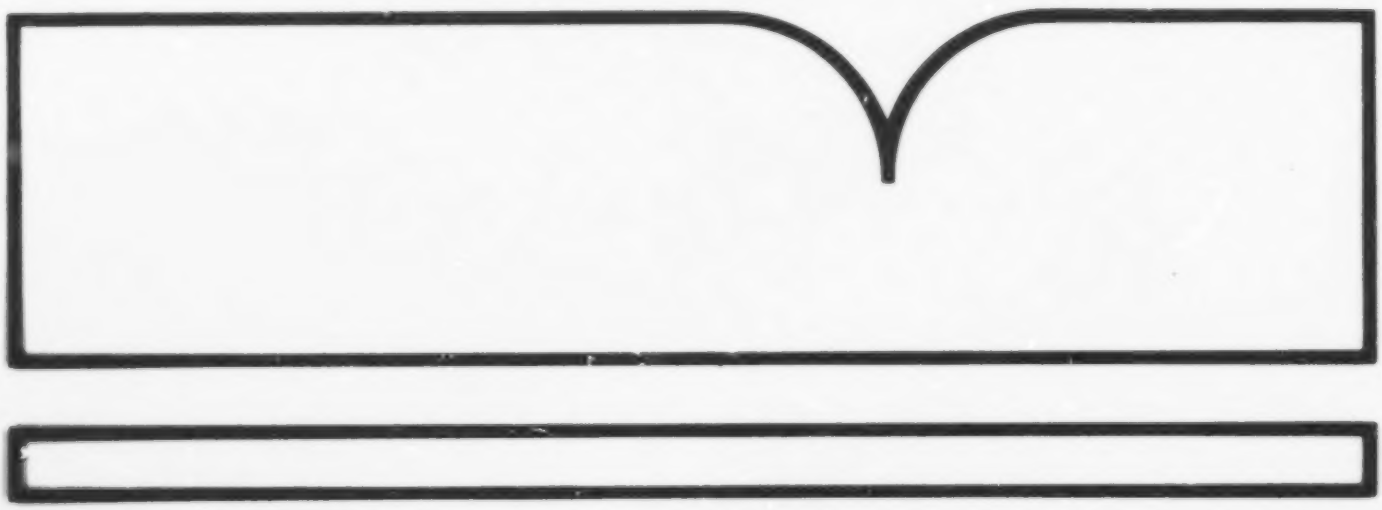

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Under the 1977 Clean Water Act, Congress mandated the U.S. Environmental Protection Agency to develop ambient water quality criteria for 129 priority Pollutants. These criteria were published in 1980. Under Section 304(a)(1) of the Clean Water Act as amended in 1987, the U.S. EPA is mandated to re-evaluate and update these criteria every five years. These addenda represent an updated literature search current as of 1988, plus additional information from Agency files and Program Offices. This addendum is to update the existing Ambient Water Quality Criteria Document for Chlorinated Phenols.

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PREFACE

Under the 1977 Clean Water Act, Congress mandated the U.S. Environmental Protection Agency to develop ambient water quality criteria for 129 priority pollutants. These criteria were published in 1980. Under Section 304(a)(1) of the Clean Water Act as amended in 1987, the U.S. EPA is mandated to re-evaluate and update these criteria every five years. These addenda represent an updated literature search current as of 1988, plus additional information from Agency files and Program Offices. The first draft of this addendum was prepared by Syracuse Research Corporation under contract no. 68-C8-0004.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BUN	Blood urea nitrogen
CRAVE	Carcinogen Risk Assessment Verification Endeavor
DMSO	Dimethyl sulfoxide
LOAEL	Lowest-observed-adverse-effect level
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
ppm	Parts per million
RfD	Reference dose
RQ	Reportable quantity
TWA	Time-weighted average

INTRODUCTION

Under Section 304(a)(1) of the Clean Water Act of 1977 as amended in 1987, the U.S. EPA is required to publish criteria for water quality accurately reflecting the latest scientific knowledge regarding the effects on health and welfare that may occur from the presence of pollutants in any body of water, including groundwater. In accordance with the 1977 act, Ambient Water Quality Criteria Documents (AWQCDs) were developed in 1980 for 65 toxic pollutants or classes of pollutants listed under Section 307(a)(1).

These addenda are intended to serve as an update of the original AWQCDs. The addenda provide the Agency with the latest scientific assessments of potential health hazards associated with these pollutants and serve as guidelines for modifying the current (1980) AWQCDs.

The human health criteria in these addenda are based on Agency verified risk assessment values when available. These values consist of reference doses (RfD) for those chemicals believed to be systemic toxicants (i.e., do not induce cancer) and cancer risk factors for those thought likely to cause cancer in humans. The verification process consists of a review and consensus of risk assessment values provided by an Agency workgroup consisting of scientists from each of the major Agency offices. Assessments for noncarcinogens are verified by the RfD workgroup and those for carcinogens are verified by the Carcinogen Risk Assessment Verification Endeavor (CRAVE) workgroup. If such values are not available, the criteria are based on the most recent Agency health assessment. In the absence of any appropriate Agency value, RfD values or cancer risk factors are derived by current Agency methods if adequate new data are available, and criteria are recommended based on the proposed RfD or risk factor.

The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is derived by dividing a NOAEL or LOAEL for subchronic or chronic exposure by standard uncertainty factor(s) times an additional uncertainty factor:

$$RfD = \frac{\text{NOAEL or LOAEL}}{UF(s) \times UF}$$

The standard uncertainty factors are applied to reflect the various types of data used to estimate RfDs. An uncertainty factor of 10 is used to account for variations in human sensitivity when extrapolating from valid human studies involving long-term exposure of average, healthy subjects. An additional 10-fold factor is used for each of the following: to extrapolate from long-term animal studies to the case of humans, to extrapolate from subchronic animal studies to chronic exposure, and to extrapolate from a LOAEL to a NOAEL. An additional uncertainty factor of >0-10 may be applied to reflect professional assessment of the uncertainties of the study and data base not explicitly addressed by the standard uncertainty factors (i.e., completeness of the overall data base). The default value for the additional uncertainty factor is 1.

In assessing the carcinogenic potential of a chemical, the U.S. EPA classifies the chemical into one of the following groups according to the degree of evidence in epidemiological studies and animal studies: Group A - Human Carcinogen; Group B - Probable Human Carcinogen [limited evidence in humans with or without sufficient evidence in animals (Group B1) or inadequate evidence in humans with sufficient evidence in animals (Group B2)]; Group C - Possible Human Carcinogen (limited evidence of carcinogenicity in animals in the absence of human data); Group D - Not Classifiable as to

Human Carcinogenicity (inadequate or no evidence); Group E - Evidence of Noncarcinogenicity for Humans. Quantitative carcinogenic risk assessments are performed for chemicals in Groups A and B, and on a case-by-case basis for chemicals in Group C. Upper-bound cancer unit risks (slope values) are estimated through the use of mathematical extrapolation models. Most commonly for animal data, the linearized multistage model with a 95% upper confidence limit is used to provide a low-dose estimate of cancer risk. The cancer risk is characterized as an upper-limit estimate (i.e., the true risk to humans, while not identifiable, is not likely to exceed the upper-limit estimate and in fact may be lower). Alternative risk models to the multistage model, such as the one-hit, Weibull, Logit or Probit model, are available and may be used when the evidence indicates that they may be more appropriate. In the absence of such evidence, the Agency recommends the linearized multistage model to provide consistency of approach and an upper-bound on the potential carcinogenic risk. In the case where human data are used for quantitative risk assessment, an upper-bound estimate rather than a 95% upper-bound estimate is used when low-dose linearity is assumed.

The AWQCD on chlorinated phenols covers isomers not addressed in separate AWQCDs (i.e., isomers other than 2-chlorophenol, 2,4-dichlorophenol and pentachlorophenol). In addition, the AWQCD on chlorinated phenols covers the methylchlorophenols, usually called chlorocresols.

REVIEW OF NEW DATA

Toxicologic/Carcinogenic Effects

Monochlorophenols (excluding 2-chlorophenol)

Ambient water quality criteria for 3-chlorophenol and 4-chlorophenol (U.S. EPA, 1980) were based upon undesirable organoleptic effects. Toxicity data were inadequate for determination of criteria based on health effects of these compounds. No new data pertinent to criterion derivation were found in the literature searched. Based on the information available, 3-chlorophenol and 4-chlorophenol could be classified in U.S. EPA Group D - not classifiable as to human carcinogenicity.

Dichlorophenols (excluding 2,4-dichlorophenol)

Ambient water quality criteria for dichlorophenols (U.S. EPA, 1980) were based upon undesirable organoleptic effects. There were inadequate toxicity data for derivation of health-effects based criteria. No new data pertinent to criterion derivation were found in the literature searched. Based on the lack of data concerning carcinogenicity, the U.S. EPA (1987a) classified dichlorophenols in Group D - not classifiable as to human carcinogenicity.

Trichlorophenols

The ambient water quality criterion for 2,4,5-trichlorophenol (U.S. EPA, 1980) was based upon undesirable organoleptic effects. A toxicity-based ambient water quality criterion was also calculated for 2,4,5-trichlorophenol, based on a 98-day rat feeding study by McCollister et al. (1961) (see Quantification of Effects section).

A screening test for carcinogenicity of 2,4,5-trichlorophenol, not reviewed in the AWQCD (U.S. EPA, 1980), was performed by BRL (1968). Groups of 18 male and 18 female B6C3F1 mice and 18 male and female B6AKF1 mice were injected with a single subcutaneous dose of 1000 mg/kg in corn oil. No

increase in incidence of tumors over that of controls was noted. Based on the information available, 2,4,5-trichlorophenol could be classified in U.S. EPA Group D - not classifiable as to human carcinogenicity.

Chernoff and Kavlock (1982) administered 2,4,5-trichlorophenol by gavage to CD-1 mice at 800 mg/kg on gestation days 8-12 and found significantly reduced ($p<0.05$) litter sizes compared with controls, but no effects were observed on maternal weight gain, survival of pups to postnatal day 3 or pup weights at postnatal days 1 and 3. Gray and Kavlock (1984) followed the growth, viability, morphology and reproductive performance of the F_1 generation from the Chernoff and Kavlock (1982) study for 250 days and the only effect noted was smaller litter size compared with controls when treated F_1 generation mice were mated.

The U.S. EPA (1986a) classified 2,4,6-trichlorophenol in Group B2 - probable human carcinogen - based on increased incidence of lymphomas or leukemias in male rats and hepatocellular carcinomas or adenomas in male and female mice (NCI, 1979); ambient water quality criteria were based on carcinogenicity. Smith et al. (1984) conducted a case-control study of the association between soft-tissue sarcoma and exposure to phenoxyherbicides or 2,4,6-trichlorophenol (which is highly skin permeable). Exposure to 2,4,6-trichlorophenol occurred in New Zealand meat works and tanneries. Smith et al. (1984) found a positive association for those exposed through meat handling or tanning of hides. Men with soft tissue sarcoma were 2.8 times more likely to have been employed in meat works and 7.2 times more likely to have worked in a pelt department or tannery than were men with other types of cancer (controls). Pearce et al. (1986), in a follow-up study, interviewed 83 cases of non-Hodgkin's lymphoma, along with 168 controls with other types of cancer and 228 general population controls. They found no

significant differences between the two control groups, nor between the cases and controls regarding potential exposure to phenoxyherbicides (i.e., through farming). The investigators found a significant increase in risk of non-Hodgkins lymphoma in meat workers exposed to chemicals including 2,4,6-trichlorophenol. Men with non-Hodgkins lymphoma were 1.8 times more likely to have been employed in meat works than were men with other types of cancer. The results of these studies are confounded, however, by multiple exposures, small study populations and lack of quantitative exposure data.

An animal study by Stoner et al. (1986) yielded negative results when 2,4,6-trichlorophenol was tested in a strain A mouse lung adenoma bioassay. Groups of 16 male and 16 female A/J mice were treated by intraperitoneal injection or gavage 3 times/week for 8 weeks. The total dose/mouse was 1200, 600 or 240 mg/kg (intraperitoneally) or 1200 mg/kg (gavage). Controls received vehicle only (tricaprylin). Mice were observed for 16 weeks post-treatment, and were then sacrificed and examined for tumors.

A screening study by BRL (1968) also reported negative findings. Groups of 18/sex B6C3F1 and B6AKF1 mice were administered 464 mg/kg 2,4,6-trichlorophenol in corn oil via single subcutaneous injection at 28 days of age, and were observed for ~18 months. The incidence of tumors did not differ from that of controls treated with corn oil only. The BRL (1968) study included results of an oral study in the same strains of mice, reviewed in the AWQCD (U.S. EPA, 1980).

Reproductive effects have been reported in a recent study by Exon and Koller (1985), who exposed groups of 12-20 female Sprague-Dawley rats to drinking water containing 0, 3, 30 or 300 ppm 2,4,6-trichlorophenol from 3 weeks of age through breeding (at 90 days with untreated males) and lactation. Litter sizes were significantly smaller ($p<0.10$) with exposures of

300 ppm, compared with controls. The percent of stillborn pups tended to be increased over controls, but the increase was not statistically significant. Progeny of dams treated as described were continued on the same drinking water concentrations received by their dams for an additional 12-15 weeks, and were then assessed for immune competence. No statistically significant effects were seen; however, antibody levels, delayed-type hypersensitivity reactions and macrophage numbers were consistently greater than controls. At 12 weeks, mean liver weights were significantly increased in a dose-related manner in progeny that received 30 and 300 ppm.

Blackburn et al. (1986) treated male Long Evans hooded rats by gavage with doses of 0, 100, 500 or 1000 mg/kg 2,4,6-trichlorophenol in corn oil, 5 days/week for 11 weeks. Semen profiles (sperm count, motility and morphology) and copulatory behavior were examined 10 weeks pre- and post-treatment. At 11 weeks, males were mated with untreated females. No effects on male reproduction were reported. The only effects observed were in the high-dose group in which a reduction in weight gain occurred and eight rats died during the first 4 weeks of treatment. Blackburn et al. (1986) also studied reproductive effects in groups of ~30 female Long-Evans hooded rats treated with 0, 100, 500 or 1000 mg/kg of 2,4,6-trichlorophenol in corn oil by gavage, 5 days/week for 2 weeks, followed by mating with untreated males. Daily dosing was continued from mating through day 21 of gestation. Body weights of high-dose females were significantly depressed during the 2 weeks pre-mating and some days during gestation. Weights of male and female pups (mean weight/litter) from the 500 and 1000 mg/kg treated groups were significantly depressed at birth, but by postnatal day 4, no differences were detected in weights of exposed or control offspring, and subsequent weight gain and survival were unaffected. The authors suggested that the

initial effect on pup weight may have been a result of a slight increase in litter size, and concluded that 2,4,6-trichlorophenol had no effect on male or female reproduction at the doses used (maximally tolerated doses).

Data pertinent to derivation of criteria for other trichlorophenol isomers were not available in 1980 (U.S. EPA, 1980) and were not located in searches of the literature published since that time.

Tetrachlorophenols

Ambient water quality criteria for tetrachlorophenols were based upon organoleptic data (taste and odor threshold) (U.S. EPA, 1980). There were inadequate toxicity data for determination of criteria based on health effects of this compound. Two subchronic studies have since been completed.

In a 55-day study by Hattula et al. (1981), 2-month-old male Wistar rats were administered 0, 10, 50 and 100 mg/kg/day 2,3,4,6-tetrachlorophenol by gavage in olive oil. The number of rats/group was not reported. The animals were sacrificed at 55 days, and samples of liver, kidney, spleen, stomach, small and large intestine, muscle and brain were examined. The only significant effects were mild dilation of the veins of the stomach mucosa at unspecified dose level(s), necrosis of the small intestines at the highest dose, and histopathologic effects on the liver at $\geq$50 mg/kg/day. At 10 mg/kg/day, no changes were observed in the parenchyma (whether other changes were noted is not clear). This study used a commercial grade compound, however, which contains substantial proportions of pentachlorophenol, dioxins and other contaminants (U.S. EPA, 1987b).

The U.S. EPA (1986b) sponsored a 90-day subchronic oral toxicity study in which 30 Sprague-Dawley rats/sex/dose were dosed with 0, 25, 100 or 200 mg/kg/day 2,3,4,6-tetrachlorophenol by gavage in olive oil. Body weight, food consumption, clinical signs of toxicity, gross (all rats) and microscopic pathology (10 rats/sex/group at ~45 days and 10 rats/sex/group at 90

days) data were monitored. No significant differences from controls were noted at 25 mg/kg/day (NOAEL), but at 100 mg/kg/day (LOAEL), there were significantly higher absolute and relative kidney weights (to body and brain) and significantly increased BUN levels in females, and significantly increased absolute and relative liver weights among both sexes. Centrilobular hypertrophy was seen during histopathologic examination of the livers of 12 males and 1 female in the 100 mg/kg/day group. At 200 mg/kg/day, body weights of the males were significantly lower than those of controls starting at week 4, absolute and relative kidney and liver weights were elevated in both sexes, and hepatic centrilobular hypertrophy was seen in 15 males and 6 females.

A teratogenicity study of 2,3,4,6-tetrachlorophenol (Research Triangle Institute, 1987) was conducted as a follow-up to the Schwetz et al. (1974) study described in the AWQCD (U.S.EPA, 1980). The Research Triangle Institute (1987) study administered 0, 25, 100 or 200 mg/kg/day of purified-grade 2,3,4,6-tetrachlorophenol in olive oil daily by gavage to pregnant rats on days 6-15 of gestation. Body weight gain, food consumption, and clinical and gross pathology data were recorded. The only adverse effect noted in this study was a significant reduction in gestational weight gain (74% of the control value) at 200 mg/kg/day. However, dams in the 100 mg/kg/day group exhibited a corrected gestational weight gain that was only 87% of the control group, so that the mid-dose appeared to approach the low effect level for this endpoint. It was noted that all treated groups consumed significantly more food than did the control group during the post-treatment period. Embryo/fetal growth and prenatal viability were not adversely affected by 2,3,4,6-tetrachlorophenol exposure, nor was any definitive evidence obtained for an effect on fetal morphological development.

As part of a screening study for carcinogenicity, BRL (1968) studied the carcinogenicity of 2,3,4,6-tetrachlorophenol in groups of 18/sex/strain B6C3F1 and B6AKF1 mice following a single subcutaneous injection of 100 mg/kg 2,3,4,6-tetrachlorophenol in DMSO. Mice were observed for ~18 months post-treatment, and no increase in incidence of tumors was found compared with controls. Based on the information available, 2,3,4,6-tetrachlorophenol could be classified in U.S. EPA Group D - not classifiable as to human carcinogenicity.

Data pertinent to the derivation of criteria for other tetrachlorophenol isomers were not available in 1980 (U.S. EPA, 1980) and were not located in searches of the literature published since that time.

Chlorocresols

The U.S. EPA (1980) based its ambient water quality criterion for the chlorocresols upon organoleptic data. Toxicity data were inadequate for determination of criteria based on health effects of these compounds. Pertinent new data regarding the toxicity or carcinogenicity of chlorocresols are limited to the following information for p-chloro-m-cresol.

The U.S. EPA (1988a) classified p-chloro-m-cresol in U.S. EPA Group D - not classifiable as to carcinogenicity potential - because of a lack of adequate human or animal data.

Madsen et al. (1986) conducted a subacute study on rats in which groups of 10/sex were treated by gavage for 28 days with 0, 50, 200 or 400 mg/kg/day p-chloro-m-cresol in soybean oil. Parameters examined included weight gain, organ weights, hematology, clinical chemistry and histopathology. The authors failed to report details of the results (other than weight gain), and stated that the only effects noted were significant decreases ($p<0.05$ for males; $p<0.01$ for females) in weight gain of treated

vs. control rats at 400 mg/kg/day (LOAEL). A NOAEL of 200 mg/kg/day was noted. Based on the information available, 4-chloro-o-cresol and 6-chloro-m-cresol could be classified in U.S. EPA Group D - not classifiable as to human carcinogenicity.

Bioconcentration Factor (BCF)

Pertinent new information concerning the bioconcentration factor for chlorinated phenols is currently undergoing Agency review. The BCFs of 8.6, 110, 150 and 240 derived for 4-chlorophenol, 2,4,5-trichlorophenol, 2,4,6-trichlorophenol and 2,3,4,6-tetrachlorophenol, respectively, will be used until this review is completed. Data were not available to derive BCFs for dichlorophenols (U.S. EPA, 1980).

QUANTIFICATION OF EFFECTS

Monochlorophenols

The existing ambient water quality criterion for both 3-chlorophenol and 4-chlorophenol is 0.1 µg/ℓ, based upon the prevention of undesirable organoleptic effects (taste threshold) as found in the study by Deitz and Traud (1978). Test amounts of 3-chlorophenol or 4-chlorophenol were added to freshwater obtained from the base outlet of the Verse Dam in Germany, and odor and taste were tested among a reasonably substantial number of subjects (9-12 for odor; 4 for taste) of both sexes and various ages. The odor threshold values were 50 µg/ℓ (3-chlorophenol) and 60 µg/ℓ (4-chlorophenol). Toxicological data were insufficient to derive criteria based upon health effects (U.S. EPA, 1980)

Because no health effects data for 3-chlorophenol or 4-chlorophenol have been located in the recent literature, no basis for determining a new ambient water quality criterion has been found. Therefore, the 1980 ambient water quality criterion for 3-chlorophenol and 4-chlorophenol of 0.1 µg/ℓ is still recommended. Data regarding mammalian health effects should be developed as a more substantial basis for setting a criterion for the protection of human health.

Dichlorophenols

The U.S. EPA (1980) derived criteria for the following dichlorophenols, based upon aesthetic effects from the study by Deitz and Traud (1978):

2,3-Dichlorophenol:	0.04 µg/ℓ
2,5-Dichlorophenol:	0.5 µg/ℓ
2,6-Dichlorophenol:	0.2 µg/ℓ
3,4-Dichlorophenol:	0.3 µg/ℓ

Toxicity data were inadequate to determine criteria based on health effects for these compounds; therefore, it is recommended that the above criteria (U.S. EPA, 1980) remain in effect.

Trichlorophenols

The U.S. EPA (1980) based the ambient water quality criterion of 1.0 µg/ℓ for 2,4,5-trichlorophenol upon organoleptic data (taste threshold) from the study by Deitz and Traud (1978). A health-effect-based criterion was also derived, based on an ADI calculated from the NOEL in a study by McCollister et al. (1961). In this study, groups of 10 male and 10 female Wistar rats were administered dietary levels of 0, 0.01, 0.03 0.1, 0.3 or 1.0% 2,4,5-trichlorophenol (99% purity), or the equivalent of 10, 30, 100, 300 or 1,000 mg/kg/day. The dose conversion from ppm in diet to mg/kg/day assumed food consumption to be equivalent to 10% of body weight in young adult rats. Effects monitored in this study were behavior, mortality, food consumption, growth, terminal hematology, body and organ weights, and gross and microscopic pathology. The NOEL was 100 mg/kg/day. Mild diuresis and slight degenerative effects in the livers and kidneys of both sexes occurred at 300 mg/kg/day, the LOAEL. Using the NOAEL of 100 mg/kg/day and an uncertainty factor of 1000 (to account for inter- and intraspecies differences and for subchronic duration), an ADI (RfD) of 7 mg/day for a 70 kg human (0.1 mg/kg/day) was calculated.

The U.S. EPA (1985) has verified this oral RfD of 0.1 mg/kg/day. Therefore, the ambient water quality criterion protective of human health remains the same as in U.S. EPA (1980), 2.6 mg/ℓ, assuming daily consumption of 2 ℓ of water and 6.5 g fish and shellfish with a BCF for 2,4,5-trichlorophenol of 110. If exposure is assumed to be from consumption of fish and shellfish alone, the criterion is 9.8 mg/ℓ.

The U.S. EPA (1980) presented an ambient water quality criterion of 2.0 µg/ℓ for 2,4,6-trichlorophenol based on organoleptic data (taste threshold) of Deitz and Traud (1978), but recommended a cancer-based criterion for the protection of human health. The recommended criteria were calculated from a q_1^* based on carcinogenicity data from an NCI (1979) study in F344 rats and B6C3F1 mice. In this study, groups of 50 male and 50 female rats were fed diets of 5000 or 10,000 ppm 2,4,6-trichlorophenol for 106 or 107 weeks. For the mouse study, groups of 50 males received the same dosages as above for 105 weeks. Groups of 50 female mice were exposed initially to 10,000 or 20,000 ppm for 38 weeks; because of the resulting excessively decreased body weights, however, doses were then reduced to 2500 and 5000 ppm for 67 weeks. The TWA doses were 5214 or 10,428 ppm for these females. Matched controls consisted of 20 animals/sex/species. 2,4,6-Trichlorophenol was carcinogenic to male rats, causing dose-related lymphomas or leukemias at significantly higher incidences in both test groups than in controls. In the mice, both sexes incurred hepatocellular carcinomas or adenomas in a dose-related pattern, with significantly higher incidences in both test groups of males and in the high-dose female group. A q_1^* of 0.01984/mg/kg/day was derived from these dose-response data for hepatocellular carcinoma and adenoma in male mice in the NCI (1979) study.

This q_1^* or slope factor, rounded to 0.02 $(mg/kg/day)^{-1}$, has been verified by U.S. EPA (1986a). Using the "unrounded" value of 0.01984 $(mg/kg/day)^{-1}$, and assuming 70 kg body weight and a daily intake of 2 ℓ of water and 6.5 g of fish and shellfish with a BCF of 150, the cancer-based

criteria for 2,4,6-trichlorophenol in ambient water remain as calculated in U.S. EPA (1980):

Exposure Assumptions (per day)	Risk Levels and Corresponding Criteria (µg/ℓ)				
	0	10^{-7}	10^{-6}	10^{-5}	10^{-4}
2 ℓ of drinking water and consumption of 6.5 g of fish and shellfish	0	0.12	1.2	12	120
Consumption of fish and shellfish only	0	0.36	3.6	36	360

It should be noted that the current verified slope factor has recently been flagged for reconsideration by the CRAVE Workgroup. These criteria will therefore be revised if necessary to reflect final Workgroup resolution.

Tetrachlorophenols

The U.S. EPA (1980) determined that data were inadequate to derive a toxicity-based criterion for any of the tetrachlorophenols. The only tetrachlorophenol for which any data existed was 2,3,4,6-tetrachlorophenol, for which a taste threshold of 1 µg/ℓ was established by Deitz and Traud (1978). The ambient water quality criterion for 2,3,4,6-tetrachlorophenol, based on prevention of adverse oganoleptic effects, was set at 1 µg/ℓ.

Since then, an oral Rfd of 0.03 mg/kg/day has been derived and verified for 2,3,4,6-tetrachlorophenol (U.S. EPA, 1987b), based on the NOAEL of 25 mg/kg/day in a recent 90-day subchronic oral toxicity study in rats (U.S. EPA, 1986b). The LOAEL of 100 mg/kg/day in this study was associated with increased liver weights and hepatic centrilobular hypertrophy. By applying an uncertainty factor of 1000 (10 for interspecies extrapolation, 10 for intraspecies variations in sensitivity and 10 for extrapolation from subchronic to chronic equivalent), an RfD of 0.025, rounded to 0.03 mg/kg/day, was derived.

The above data and verified RfD support derivation of a health effects-based criterion for 2,3,4,6-tetrachlorophenol. Using the "unrounded" value of the verified oral RfD, 0.025 mg/kg/day, and assuming a 70 kg body weight, daily consumption of 2 ℓ of water and 6.5 g fish and shellfish with a BCF for 2,3,4,6-tetrachlorophenol of 240 (U.S. EPA, 1980), a new ambient water quality criterion of 0.49 mg/ℓ, based on health effects, is derived. If exposure is through consumption of fish and shellfish alone, the criterion is 3.13 mg/ℓ.

Chlorocresols

The U.S. EPA (1980) derived criteria for the following chlorocresols, based upon aesthetic effects from the study by Deitz and Traud (1978):

4-chloro-o-cresol (2-methyl-4-chlorophenol):	1.8 mg/ℓ
6-chloro-m-cresol (3-methyl-6-chlorophenol):	20 µg/ℓ
4-chloro-m-cresol (3-methyl-4-chlorophenol): (p-chloro-m-cresol)	3.0 mg/ℓ

Toxicity data were inadequate to determine criteria based on health effects for these compounds; therefore, it is recommended that the above criteria (U.S. EPA, 1980) remain in effect.

EXISTING STANDARDS AND CRITERIA

Monochlorophenols

Criteria and standards other than ambient water quality criteria (see Quantification of Effects section) have not been established for these compounds.

Dichlorophenols

Criteria and standards other than ambient water quality criteria (see Quantification of Effects section) have not been established for these compounds.

Trichlorophenols

The U.S. EPA (1986c) stated that all uses of 2,4,5-trichlorophenol have been voluntarily cancelled or suspended in response to the RPAR issued by U.S. EPA in 1978, which concerned oncogenicity and fetotoxicity data for TCDD, a common contaminant in 2,4,5-trichlorophenol; additional exposure data were requested (U.S. EPA, 1987a).

A verified oral RfD for 2,4,5-trichlorophenol of 0.1 mg/kg/day has been established by the U.S. EPA (1985) based on a NOEL of 100 mg/kg/day for rats in a subchonic feeding study by McCollister et al. (1961). An uncertainty factor of 1000 was applied.

The U.S. EPA (1986a) has verified a slope factor of 0.02 $(mg/kg/day)^{-1}$ and a drinking water unit risk of $5.7 \times 10^{-7}/\mu g/l$ for 2,4,6-trichlorophenol, based on dose-response data for hepatocellular carcinoma and adenoma in mice fed the chemical in the diet (NCI, 1979). WHO (1984) established a drinking water guideline value for 2,4,6-trichlorophenol of 10 µg/l, based on a "linear multi-stage extrapolation" of carcinogenicity data.

RQs of 10 pounds have been proposed for 2,4,5- and 2,4,6-trichlorophenol, based on aquatic toxicity data U.S. EPA (1988b,c).

Tetrachlorophenols

The U.S. EPA (1987b) has established a verified oral RfD of 0.03 mg/kg/day for 2,3,4,6-tetrachlorophenol, derived from a 90-day rat feeding study (U.S. EPA, 1987a). This replaced the former oral RfD of 0.01 mg/kg/day, verified in 1985 and based on a 55-day oral study by Hattula et al. (1981), which was judged less adequate because commercial grade compound containing substantial amounts of contaminants such as pentachlorophenol and dioxins was used. Also, low numbers of animals and short study duration reduced confidence in the data.

The U.S. EPA (1988d) has established an RQ of 10 pounds for 2,3,4,6-tetrachlorophenol, based on aquatic toxicity.

Chlorocresols

Other than ambient water quality criteria, no criteria and standards have been established for the chlorocresols.

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